

PATENT COOPERATION TREATY

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From the INTERNATIONAL SEARCHING AUTHORITY

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PATENT RECORDS
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To:

E.I. DUPONT DE NEMOURS AND COMPANY
Legal Patent Records Center
Attn. FELTHAM, N.
1007 Market Street
Wilmington, Delaware 19805
UNITED STATES OF AMERICA

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

6/8/01 - ref's for search in US

JUN 07 2001

Date of mailing
(day/month/year)

28/05/2001

Applicant's or agent's file reference

BC1019PCT

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 00/ 25856

International filing date
(day/month/year)

21/09/2000

Applicant

E.I. DU PONT DE NEMOURS AND COMPANY

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Doreen Golze

[Signature]

REY NOTED

NOTES FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference BC1019PCT	FOR FURTHER ACTION		see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US 00/ 25856	International filing date (day/month/year) 21/09/2000	(Earliest) Priority Date (day/month/year) 21/09/1999	
Applicant E. I. DU PONT DE NEMOURS AND COMPANY			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☒ because this figure better characterizes the invention.

4

☐ None of the figures.

INTEF TIONAL SEARCH REPORT

International Application No.
P 00/25856

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/54 C12N9/10 C12N15/82 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, STRAND, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EMBL Database, Heidelberg, FRG Empln accession number AB023482 15 March 1999 SASAKI, T. ET AL.: "Oryza sativa genomic DNA, chromosome 6, clone P0680A03" XP002167058	1,3,4
Y	the whole document ---	2
X	EMBL Database, Heidelberg, FRG Empln accession number AB020755 14 December 1998 NAKAMURA, Y.: "Arabidopsis thaliana genomic DNA, chromosome 5, P1 clone: MZNI" XP002160876	1,3
Y	the whole document ---	2,4
	-/--	

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *I* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *(*) document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *8* document member of the same patent family

Date of the actual completion of the international search

10 May 2001

Date of mailing of the international search report

28.05.01

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax. (+31-70) 340-3016

Authorized officer

Fuchs, U

INTERNATIONAL SEARCH REPORT

I. International Application No.
P. 00/25856

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EMBL Database, Heidelberg, FRG Empln accession number AB011483 10 March 1998 NAKAMURA, Y.: "Arabidopsis thaliana genomic DNA, chromosome 5, P1 clone: MUF9" XP002160878 cited in the application	1,3
Y	the whole document ---	2,4
X	EMBL Database, Heidelberg, FRG Empln accession number AC007584 19 May 1999 LIN, X. ET AL.: "Arabidopsis thaliana chromosome II section 101 of 255 of the complete sequence. Sequence from clones MJB20, T19E12" XP002167059	1,3
Y	the whole document ---	2,4
X	EMBL Database, Heidelberg, FRG Emest_Pln2 accession number AI965398 24 August 1999 SHOEMAKER, R. ET AL.: "sc71b10.y1 Gm-c1016 Glycine max cDNA clone GENOME SYSTEMS CLONE ID: Gm-c1016-1844 5' similar to SW: Y506_SYNY3 Q55482 HYPOTHETICAL 28.8 KD PROTEIN SLL0506, mRNA sequence" XP002167060	1,3
Y	the whole document ---	2,4
X	EMBL Database, Heidelberg, FRG Emest_Pln2 accession number AU069089 07 June 1999 SASAKI, T.: "Oryza sativa cDNA, partial sequence (C52041_1A)" XP002160877	1
A	the whole document ---	13-15
X	EMBL Database, Heidelberg, FRG Emest_Pln4 accession number AW038635 17 September 1999 D'ASCENZO, M. ET AL.: "EST280318 tomato mixed elicitor, BTI Lycopersicon esculentum cDNA clone cLET7I9, mRNA sequence" XP002167061	1
A	the whole document ---	13-15
	-/--	

INTERNATIONAL SEARCH REPORT

International Application No.
P 00/25856

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	APFEL, C.M. ET AL.: "Use of Genomics To Identify Bacterial Undecaprenyl Pyrophosphate Synthetase" JOURNAL OF BACTERIOLOGY, vol. 181, no. 2, January 1999 (1999-01), pages 483-492, XP002160874 cited in the application	2,4
A	abstract page 486 -page 487; figure 3 page 488, column 1, line 7 -column 2, line 3 page 490, column 2, line 36 - line 64	1,3,5-15
A	SHIMIZU, N. ET AL.: "Molecular Cloning, Expression, and Purification of Undecaprenyl Diphosphate Synthase" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 31, 31 July 1998 (1998-07-31), pages 19476-19481, XP002160875 cited in the application the whole document	1-15
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; PHYTOCHEMICAL ANALYSIS, vol. 8, no. 3, 1997 CORNISH, K. & BARTLETT, D.L.: "Stabilisation of particle integrity and particle bound cis-prenyl transferase activity in stored, purified rubber particles" XP002161336 abstract	1-15

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-15 partially

An isolated nucleic acid fragment encoding a plant cis-prenyltransferase polypeptide selected from the group consisting of a) an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence SEQ ID NO: 2, b) an isolated nucleic acid fragment that is substantially similar to an isolated nucleic acid fragment encoding all or a substantial portion of SEQ ID NO: 2, c) an isolated nucleic acid fragment derived from *Dimorphotheca* encoding a polypeptide having at least 41% identity with the amino acid sequence SEQ ID NO: 24, d) an isolated nucleic acid fragment derived from *Dimorphotheca* having at least 50% identity with the nucleic acid sequence SEQ ID NO: 23, e) an isolated nucleic acid fragment that hybridizes with said nucleic acid sequences, f) an isolated nucleic acid fragment that hybridizes with the nucleic acid sequence SEQ ID NO: 1, g) an isolated nucleic acid fragment that is complementary to said nucleic acid sequences, said isolated nucleic acid fragment having the nucleic acid sequence SEQ ID NO: 1, a polypeptide encoded by said isolated nucleic acid fragment, said polypeptide having the amino acid sequence SEQ ID NO: 2, a method of obtaining a nucleic acid fragment encoding all or a substantial portion of the amino acid sequence of a plant cis-prenyltransferase polypeptide comprising a hybridization step involving said nucleic acid fragment, a method of obtaining a nucleic acid fragment encoding all or a substantial portion of the amino acid sequence of a plant cis-prenyltransferase polypeptide comprising a cDNA amplification step involving primers corresponding to a portion of SEQ ID NO: 1, a chimeric gene comprising said nucleic acid fragment, a transformed host cell comprising said chimeric gene and a method of altering the level of expression of a plant cis-prenyltransferase polypeptide in a host cell;

2. Claims: 1-15 partially

Idem as subject 1 but limited to *Calendula officinalis* and SEQ ID NOS: 3 and 4;

3. Claims: 1-15 partially

Idem as subject 1 but limited to *Hevea brasiliensis* and SEQ ID NOS: 5-10;

4. Claims: 1-15 partially

Idem as subject 1 but limited to *Vitis* sp. and SEQ ID NOS:

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

11 and 12;

5. Claims: 1-15 partially

Idem as subject 1 but limited to *Oryza sativa* and SEQ ID NOS: 13-16;

6. Claims: 1-15 partially

Idem as subject 1 but limited to *Glycine max* and SEQ ID NOS: 17 and 18;

7. Claims: 1-15 partially

Idem as subject 1 but limited to *Triticum aestivum* and SEQ ID NOS: 19 and 20.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/25856

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

DEC 15 2001

**PATENT RECORDS
CENTER**

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

To:

FELTHAM, Neil S.
E.I. DUPONT DE NEMOURS AND COMPANY
Legal Patent Records Center
1007 Market Street
Wilmington, Delaware 19805
ETATS-UNIS D'AMERIQUE

Date of mailing
(day/month/year)

07.12.2001

Applicant's or agent's file reference
BC1019PCT

IMPORTANT NOTIFICATION

International application No.
PCT/US00/25856

International filing date (day/month/year)
21/09/2000

Priority date (day/month/year)
21/09/1999

Applicant

E.I. DU PONT DE NEMOURS AND COMPANY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Sülberg, A

Tel. +49 89 2399-7548

KEY NOTED




21 MR 2002

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BC1019PCT		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/25856	International filing date (day/month/year) 21/09/2000	Priority date (day/month/year) 21/09/1999	
International Patent Classification (IPC) or national classification and IPC C07K14/00			
Applicant E.I. DU PONT DE NEMOURS AND COMPANY			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 3 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 			
Date of submission of the demand 04/04/2001		Date of completion of this report 07.12.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Ury, A Telephone No. +49 89 2399 8411	



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25856

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*):

Description, pages:

1-32 as originally filed

Claims, No.:

1-15 as originally filed

Drawings, sheets:

1/24-24/24 as originally filed

Sequence listing part of the description, pages:

1-22, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25856

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 2, 4-14

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25856

	No:	Claims	1, 3
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations **see separate sheet**

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

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EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/25856

ITEM V.

Reference is made to the following documents:

- D1: EMBL Database, Heidelberg, FRG Empln accession number AB023482 15 March 1999 SASAKI, T. ET AL.: 'Oryza sativa genomic DNA, chromosome 6, clone P0680A03' XP002167058
- D2: EMBL Database, Heidelberg, FRG Empln accession number AB020755 14 December 1998 NAKAMURA, Y.: 'Arabidopsis thaliana genomic DNA, chromosome 5, P1 clone: MZN1' XP002160876
- D3: EMBL Database, Heidelberg, FRG Empln accession number AB011483 10 March 1998 NAKAMURA, Y.: 'Arabidopsis thaliana genomic DNA, chromosome 5, P1 clone: MUF9' XP002160878 cited in the application
- D8: APFEL, C.M. ET AL.: 'Use of Genomics To Identify Bacterial Undecaprenyl Pyrophosphate Synthetase' JOURNAL OF BACTERIOLOGY, vol. 181, no. 2, January 1999 (1999-01), pages 483-492, XP002160874 cited in the application

Novelty.

- 1. D2 discloses a nucleic acid (NA) fragment encoding plant (*Arabidopsis thaliana*) cis-prenyltransferases. 3 proteins (i.e. Q9LUY1, Q9LUY2 and Q9LUY3) which are cis-prenyltransferases homologs are deduced from this nucleic acid fragment.
 - 1.1.1 The cis-prenyltransferase of SEQ ID NO: 2 has 61,3% identity in 142 aa overlap and 55% identity in 231 aa overlap with Q9LUY1 of D2. The cis-prenyltransferase of SEQ ID NO: 2 has 47,4% identity in 232 aa overlap with Q9LUY2 of D2 and 51,4% identity in 222 aa overlap with Q9LUY3 of D2.
 - 1.1.2 Thus, the NA fragment of D2 would fall within the scope of claim 1 (d) and (e), in view of the hybridization conditions. This destroys the novelty of claim 1(d) and (e).

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1.1.3 The 3 proteins (i.e. Q9LUY1, Q9LUY2 and Q9LUY3) cis-prenyltransferases homologs of D2, also fall within the scope of present claim 3. Claim 3 is therefore not novel.

1.2.1 The cis-prenyltransferase of SEQ ID NO: 12 has 61,7% identity in 128 aa overlap and 49,8% identity in 273 aa overlap with Q9LUY1 of D2.
The cis-prenyltransferase of SEQ ID NO: 12 has 49,1% identity in 234 aa overlap with Q9LUY2 of D2.
The cis-prenyltransferase of SEQ ID NO: 12 has 57,8% identity in 128 aa overlap and 50,1% identity in 224 aa overlap with Q9LUY3 of D2.

1.2.2 Thus, the NA fragment of D2 would fall within the scope of claim 1 (d) and (e), in view of the hybridization conditions.
This destroys the novelty of claim 1(d) and (e).

1.2.3 The 3 proteins (i.e. Q9LUY1, Q9LUY2 and Q9LUY3) cis-prenyltransferases homologs of D2, also falls within the scope of present claim 3. Claim 3 is therefore not novel.

1.3.1 The cis-prenyltransferase of SEQ ID NO: 18 has 60,4% identity in 149 aa overlap and 55,8% identity in 233 aa overlap with Q9LUY1 of D2.
The cis-prenyltransferase of SEQ ID NO: 18 has 56,5% identity in 147 aa overlap and 53,6% identity in 224 aa overlap with Q9LUY3 of D2.

1.3.2 Thus, the NA fragment of D2 would fall within the scope of claim 1 (d) and (e), in view of the hybridization conditions.
This destroys the novelty of claim 1(d) and (e).

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- 1.4.1 The cis-prenyltransferase of SEQ ID NO: 20 has 52,6% identity in 152 aa overlap and 49,6% identity in 232 aa overlap with Q9LUY1 of D2.
The cis-prenyltransferase of SEQ ID NO: 20 has 49,7% identity in 153 aa overlap and 48,2% identity in 224 aa overlap with Q9LUY3 of D2.
The cis-prenyltransferase of SEQ ID NO: 20 has 47,4% identity in 232 aa overlap with Q9LUY2 of D2.
- 1.4.2 Thus, the NA fragment of D2 would fall within the scope of claim 1 (d) and (e), in view of the hybridization conditions.
This destroys the novelty of claim 1(d) and (e).
- 1.4.3 The 3 proteins (i.e. Q9LUY1, Q9LUY2 and Q9LUY3) cis-prenyltransferases homologs of D2, also falls within the scope of present claim 3. Claim 3 is therefore not novel.
2. D3 discloses a nucleic acid (NA) fragment encoding plant (*Arabidopsis thaliana*) cis-prenyltransferases. 2 proteins which are cis-prenyltransferases homologs are deduced from this nucleic acid fragment.
- 2.1.1 The cis-prenyltransferases of SEQ ID NO:6 and SEQ ID NO:8 have 46.2% identity in 171 aa overlap and 43% identity in 272 aa overlap with the cis-prenyltransferase protein of D3.

The cis-prenyltransferase of SEQ ID NO: 10 has 43,8% identity in 176 aa overlap, 42,5% identity in 280 aa overlap and 41,3% identity in 293 aa overlap with the cis-prenyltransferase protein of D3.
- 2.1.2 Thus, the NA fragment of D3 would fall within the scope of claim 1 (d) and (e), in view of the hybridization conditions.
This destroys the novelty of claim 1(d) and (e).
- 2.1.3 The 2 cis-prenyltransferases homologs of D3, also fall within the scope of present claim 3. Claim 3 is therefore not novel.

Inventive step.

- 3.1 The closest prior art is represented by D2 and D3 which disclose cis-prenyltransferases homologs from plants (*Arabidopsis thaliana*).

In the light of this prior art, the problem underlying the present application can be seen in the provision of further cis-prenyltransferases homologs from plants.

Document D8 discloses the aa sequences of 28 cis-prenyltransferases, including 25 from bacteria, and in eukaryotic genomes, 2 from *S. cerevisiae* and 1 from *C. elegans*. These protein sequences (Fig.3) reveal at least 5 strongly conserved regions where aa were identical or nearly identical in all 28 sequences. These highly conserved regions are numbered I to V in Fig.3 and consensus patterns are derived for each region.

In addition, a partial sequence which showed very good homology especially to the strongly conserved regions at the C-term end (boxes IV and V) was found in an in-house human database (D8, page 490, second to last paragraph).

On the other hand, it can be seen from D2 and D3 which disclose cis-prenyltransferases homologs from plants (*Arabidopsis thaliana*), that the above mentioned 5 strongly conserved regions I to V are also present in the plant aa sequences.

Thus, it appears that all the cis-prenyltransferase sequences (from bacteria to plants and humans) have the same 5 strongly conserved regions.

Consequently, in order to solve the underlying problem, the skilled person would have, as a matter of routine, searched (in plant cDNA or genomic libraries or in databases) other plant sequences also having said 5 strongly conserved regions. Using this approach he would have found without any inventive skill all the plant cis-prenyltransferases according to the present application.

Consequently, the subject-matter of present claims 1-4 does not involve an inventive step (Article 33.3 PCT).

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- 3.2 Claims 5-14 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.
- 3.3 The attention of the Applicant is also drawn to the fact that the alleged cis-prenyltransferase activity of all the claimed sequences is merely based on their homology with previously identified sequences in microbes. Since no cis-prenyltransferase activity has been experimentally determined for any of the claimed proteins they remain putative cis-prenyltransferases. In the absence of further evidence concerning said activity, inventive step can hardly be acknowledged since some or all of the claimed protein might actually not have the cis-prenyltransferase activity and would therefore not represent a solution to the above mentioned technical problem (Article 33.3 PCT).

ITEM VIII.

The term "encoding", in the context of claim 1(c), has no meaning and leave the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

JC13 Rec'd PCT/PTO 19 FEB 2002

CLAIMS

What is claimed is:

1. An isolated nucleic acid fragment encoding a plant *cis*-prenyltransferase protein selected from the group consisting of:

- 5 (a) an isolated nucleic acid fragment encoding the amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20;
- 10 (b) an isolated nucleic acid fragment encoding a polypeptide, the polypeptide having at least 41% identity with the amino acid sequence set forth in SEQ ID NO:24;
- (c) an isolated nucleic acid fragment encoding having at least 50% identity with nucleic acid sequence as set forth in SEQ ID
- 15 NO:23;
- (d) an isolated nucleic acid molecule that hybridizes with a nucleic acid sequence of (a) (b) or (c) under the following hybridization conditions: 0.1X SSC, 0.1% SDS, 65°C and washed with 2X SSC, 0.1% SDS followed by 0.1X SSC, 0.1% SDS; and
- 20 (e) an isolated nucleic acid fragment that hybridizes with a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:17 and SEQ ID NO:19 under the following hybridization conditions:
- 25 0.1X SSC, 0.1% SDS, 65°C and washed with 2X SSC, 0.1% SDS followed by 0.1X SSC, 0.1% SDS; or
- an isolated nucleic acid fragment that is complementary to (a), (b), (c), (d), or (e).

2. The isolated nucleic acid fragment of Claim 1 selected from the group

30 consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:17 and SEQ ID NO:19.

3. A polypeptide encoded by the isolated nucleic acid fragment of Claim 1.

4. The polypeptide of Claim 3 selected from the group consisting of

35 SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20.

5. A chimeric gene comprising the isolated nucleic acid fragments of Claim 1 operably linked to suitable regulatory sequences.

6. A transformed host cell comprising a host cell and the chimeric gene of Claim 5.

7. The transformed host cell of Claim 6 wherein the host cell is selected from the group consisting of plant cells and microbial cells.

5 8. A host cell according to Claim 7 selected from the group consisting of tobacco (*Nicotiana* spp.), tomato (*Lycopersicon* spp.), potato (*Solanum* spp.), hemp (*Cannabis* spp.), sunflower (*Helianthus* spp.), sorghum (*Sorghum vulgare*), wheat (*Triticum* spp.), maize (*Zea mays*), rice (*Oryza sativa*), rye (*Secale cereale*), oats (*Avena* spp.), barley (*Hordeum vulgare*), rapeseed (*Brassica* spp.),
10 broad bean (*Vicia faba*), french bean (*Phaseolus vulgaris*), other bean species (*Vigna* spp.), lentil (*Lens culinaris*), soybean (*Glycine max*), arabidopsis (*Arabidopsis thaliana*), guayule (*Parthenium argentatum*), cotton (*Gossypium hirsutum*), petunia (*Petunia hybrida*), flax (*Linum usitatissimum*) and carrot (*Daucus carota sativa*).

15 9. The transformed host cell of Claim 7 wherein the host cell is selected from the group consisting of *Aspergillus*, *Saccharomyces*, *Pichia*, *Candida*, *Hansenula*, *Bacillus*, *Escherichia*, *Salmonella* and *Shigella*

10. A method of altering the level of expression of a plant *cis*-prenyltransferase protein in a host cell comprising:

20 (a) transforming a host cell with the chimeric gene of Claim 6 and;
(b) growing the transformed host cell produced in step (a) under conditions that are suitable for expression of the chimeric gene resulting in production of altered levels of a plant *cis*-prenyltransferase protein in the transformed host cell relative to
25 expression levels of an untransformed host cell.

11. A method according to Claim 10 wherein the host cell is a plant cell selected from the group consisting of tobacco (*Nicotiana* spp.), tomato (*Lycopersicon* spp.), potato (*Solanum* spp.), hemp (*Cannabis* spp.), sunflower (*Helianthus* spp.), sorghum (*Sorghum vulgare*), wheat (*Triticum* spp.), maize
30 (*Zea mays*), rice (*Oryza sativa*), rye (*Secale cereale*), oats (*Avena* spp.), barley (*Hordeum vulgare*), rapeseed (*Brassica* spp.), broad bean (*Vicia faba*), french bean (*Phaseolus vulgaris*), other bean species (*Vigna* spp.), lentil (*Lens culinaris*), soybean (*Glycine max*), arabidopsis (*Arabidopsis thaliana*), guayule (*Parthenium argentatum*), cotton (*Gossypium hirsutum*), petunia (*Petunia*
35 *hybrida*), flax (*Linum usitatissimum*) and carrot (*Daucus carota sativa*).

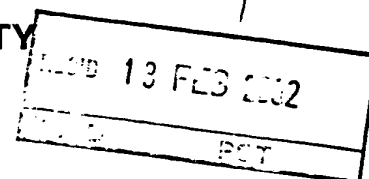
12. A method according to Claim 11 wherein the altering the level of expression of a plant *cis*-prenyltransferase protein results in a modulation in the defense mechanism of the plant.

13. A method of obtaining a nucleic acid fragment encoding the amino acid sequence encoding a plant *cis*-prenyltransferase protein comprising:

- (a) probing a cDNA or genomic library with the nucleic acid fragments of Claim 1;
- (b) identifying a DNA clone that hybridizes with the nucleic acid fragments of Claim 1; and
- (c) sequencing the cDNA or genomic fragment that comprises the clone identified in step (b), wherein the sequenced cDNA or genomic fragment encodes a plant *cis*-prenyltransferase protein.

14. A method of obtaining a nucleic acid fragment encoding the amino acid sequence encoding a plant *cis*-prenyltransferase protein comprising:

- (a) synthesizing at least one oligonucleotide primer corresponding to a portion of the sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, , SEQ ID NO:15, SEQ ID NO:17 and SEQ ID NO:19;
- (b) amplifying a cDNA insert present in a cloning vector using the oligonucleotide primer of step (a); wherein the amplified cDNA insert encodes a plant *cis*-prenyltransferase protein.



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BC1019PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/25856	International filing date (day/month/year) 21/09/2000	Priority date (day/month/year) 21/09/1999
International Patent Classification (IPC) or national classification and IPC C07K14/00		
Applicant E.I. DU PONT DE NEMOURS AND COMPANY		



1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 04/04/2001	Date of completion of this report 07.12.2001
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Ury, A Telephone No. +49 89 2399 8411 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/25856

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-32 as originally filed

Claims, No.:

1-14 as received on 06/11/2001 with letter of 06/11/2001

Drawings, sheets:

1/24-24/24 as originally filed

Sequence listing part of the description, pages:

1-22, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/25856

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
☒ paid additional fees.
☐ paid additional fees under protest.
☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 2, 4-14

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/25856

	No:	Claims	1, 3
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations
see separate sheet

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

ITEM V.

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Novelty.

1. D2 discloses a nucleic acid (NA) fragment encoding plant (*Arabidopsis thaliana*) cis-prenyltransferases. 3 proteins (i.e. Q9LUY1, Q9LUY2 and Q9LUY3) which are cis-prenyltransferases homologs are deduced from this nucleic acid fragment.
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- 3.1 The closest prior art is represented by D2 and D3 which disclose cis-prenyltransferases homologs from plants (*Arabidopsis thaliana*).

In the light of this prior art, the problem underlying the present application can be seen in the provision of further cis-prenyltransferases homologs from plants.

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On the other hand, it can be seen from D2 and D3 which disclose cis-prenyltransferases homologs from plants (*Arabidopsis thaliana*), that the above mentioned 5 strongly conserved regions I to V are also present in the plant aa sequences.

Thus, it appears that all the cis-prenyltransferase sequences (from bacteria to plants and humans) have the same 5 strongly conserved regions.

Consequently, in order to solve the underlying problem, the skilled person would have, as a matter of routine, searched (in plant cDNA or genomic libraries or in databases) other plant sequences also having said 5 strongly conserved regions. Using this approach he would have found without any inventive skill all the plant cis-prenyltransferases according to the present application.

Consequently, the subject-matter of present claims 1-4 does not involve an inventive step (Article 33.3 PCT).

- 3.2 Claims 5-14 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.
- 3.3 The attention of the Applicant is also drawn to the fact that the alleged cis-prenyltransferase activity of all the claimed sequences is merely based on their homology with previously identified sequences in microbes. Since no cis-prenyltransferase activity has been experimentally determined for any of the claimed proteins they remain putative cis-prenyltransferases. In the absence of further evidence concerning said activity, inventive step can hardly be acknowledged since some or all of the claimed protein might actually not have the cis-prenyltransferase activity and would therefore not represent a solution to the above mentioned technical problem (Article 33.3 PCT).

ITEM VIII.

The term "encoding", in the context of claim 1(c), has no meaning and leave the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

CLAIMS

What is claimed is:

1. An isolated nucleic acid fragment encoding a plant *cis*-prenyltransferase protein selected from the group consisting of:

- 5 (a) an isolated nucleic acid fragment encoding the amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20;
- 10 (b) an isolated nucleic acid fragment encoding a polypeptide, the polypeptide having at least 41% identity with the amino acid sequence set forth in SEQ ID NO:24;
- (c) an isolated nucleic acid fragment encoding having at least 50% identity with nucleic acid sequence as set forth in SEQ ID
- 15 NO:23;
- (d) an isolated nucleic acid molecule that hybridizes with a nucleic acid sequence of (a) (b) or (c) under the following hybridization conditions: 0.1X SSC, 0.1% SDS, 65°C and washed with 2X SSC, 0.1% SDS followed by 0.1X SSC, 0.1% SDS; and
- 20 (e) an isolated nucleic acid fragment that hybridizes with a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:17 and SEQ ID NO:19 under the following hybridization conditions:
- 25 0.1X SSC, 0.1% SDS, 65°C and washed with 2X SSC, 0.1% SDS followed by 0.1X SSC, 0.1% SDS; or
- an isolated nucleic acid fragment that is complementary to (a), (b), (c), (d), or (e).

2. The isolated nucleic acid fragment of Claim 1 selected from the group

30 consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, SEQ ID NO:17 and SEQ ID NO:19.

3. A polypeptide encoded by the isolated nucleic acid fragment of Claim 1.

4. The polypeptide of Claim 3 selected from the group consisting of

35 SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20.

5. A chimeric gene comprising the isolated nucleic acid fragments of Claim 1 operably linked to suitable regulatory sequences.

6. A transformed host cell comprising a host cell and the chimeric gene of Claim 5.

7. The transformed host cell of Claim 6 wherein the host cell is selected from the group consisting of plant cells and microbial cells.

5 8. A host cell according to Claim 7 selected from the group consisting of tobacco (*Nicotiana* spp.), tomato (*Lycopersicon* spp.), potato (*Solanum* spp.), hemp (*Cannabis* spp.), sunflower (*Helianthus* spp.), sorghum (*Sorghum vulgare*), wheat (*Triticum* spp.), maize (*Zea mays*), rice (*Oryza sativa*), rye (*Secale cereale*), oats (*Avena* spp.), barley (*Hordeum vulgare*), rapeseed (*Brassica* spp.),
10 broad bean (*Vicia faba*), french bean (*Phaseolus vulgaris*), other bean species (*Vigna* spp.), lentil (*Lens culinaris*), soybean (*Glycine max*), arabidopsis (*Arabidopsis thaliana*), guayule (*Parthenium argentatum*), cotton (*Gossypium hirsutum*), petunia (*Petunia hybrida*), flax (*Linum usitatissimum*) and carrot (*Daucus carota sativa*).

15 9. The transformed host cell of Claim 7 wherein the host cell is selected from the group consisting of *Aspergillus*, *Saccharomyces*, *Pichia*, *Candida*, *Hansenula*, *Bacillus*, *Escherichia*, *Salmonella* and *Shigella*

10. A method of altering the level of expression of a plant *cis*-prenyltransferase protein in a host cell comprising:

- 20 (a) transforming a host cell with the chimeric gene of Claim 6 and;
(b) growing the transformed host cell produced in step (a) under conditions that are suitable for expression of the chimeric gene resulting in production of altered levels of a plant *cis*-prenyltransferase protein in the transformed host cell relative to
25 expression levels of an untransformed host cell.

11. A method according to Claim 10 wherein the host cell is a plant cell selected from the group consisting of tobacco (*Nicotiana* spp.), tomato (*Lycopersicon* spp.), potato (*Solanum* spp.), hemp (*Cannabis* spp.), sunflower (*Helianthus* spp.), sorghum (*Sorghum vulgare*), wheat (*Triticum* spp.), maize
30 (*Zea mays*), rice (*Oryza sativa*), rye (*Secale cereale*), oats (*Avena* spp.), barley (*Hordeum vulgare*), rapeseed (*Brassica* spp.), broad bean (*Vicia faba*), french bean (*Phaseolus vulgaris*), other bean species (*Vigna* spp.), lentil (*Lens culinaris*), soybean (*Glycine max*), arabidopsis (*Arabidopsis thaliana*), guayule (*Parthenium argentatum*), cotton (*Gossypium hirsutum*), petunia (*Petunia*
35 *hybrida*), flax (*Linum usitatissimum*) and carrot (*Daucus carota sativa*).

12. A method according to Claim 11 wherein the altering the level of expression of a plant *cis*-prenyltransferase protein results in a modulation in the defense mechanism of the plant.

13. A method of obtaining a nucleic acid fragment encoding the amino acid sequence encoding a plant *cls*-prenyltransferase protein comprising:

- (a) probing a cDNA or genomic library with the nucleic acid fragments of Claim 1;
- (b) identifying a DNA clone that hybridizes with the nucleic acid fragments of Claim 1; and
- (c) sequencing the cDNA or genomic fragment that comprises the clone identified in step (b), wherein the sequenced cDNA or genomic fragment encodes a plant *cls*-prenyltransferase protein.

14. A method of obtaining a nucleic acid fragment encoding the amino acid sequence encoding a plant *cis*-prenyltransferase protein comprising:

- (a) synthesizing at least one oligonucleotide primer corresponding to a portion of the sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, , SEQ ID NO:15, SEQ ID NO:17 and SEQ ID NO:19;
- (b) amplifying a cDNA insert present in a cloning vector using the oligonucleotide primer of step (a); wherein the amplified cDNA insert encodes a plant *cis*-prenyltransferase protein.

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 02 July 2001 (02.07.01)	
International application No. PCT/US00/25856	Applicant's or agent's file reference BC1019PCT
International filing date (day/month/year) 21 September 2000 (21.09.00)	Priority date (day/month/year) 21 September 1999 (21.09.99)
Applicant COLDREN, Chris et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
04 April 2001 (04.04.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer >

Pascal Piriou

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference BC1019PCT	FOR FURTHER ACTION		see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US 00/ 25856	International filing date (day/month/year) 21/09/2000	(Earliest) Priority Date (day/month/year) 21/09/1999	
Applicant E. I. DU PONT DE NEMOURS AND COMPANY			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☒ because this figure better characterizes the invention.

4

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

P 00/25856

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/54 C12N9/10 C12N15/82 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, STRAND, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EMBL Database, Heidelberg, FRG Empln accession number AB023482 15 March 1999 SASAKI, T. ET AL.: "Oryza sativa genomic DNA, chromosome 6, clone P0680A03" XP002167058	1,3,4
Y	the whole document ---	2
X	EMBL Database, Heidelberg, FRG Empln accession number AB020755 14 December 1998 NAKAMURA, Y.: "Arabidopsis thaliana genomic DNA, chromosome 5, P1 clone: MZN1" XP002160876	1,3
Y	the whole document ---	2,4
	--- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

10 May 2001

Date of mailing of the international search report

28.05.01

Name and mailing address of the ISA

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Fuchs, U

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/25856

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EMBL Database, Heidelberg, FRG Empln accession number AB011483 10 March 1998 NAKAMURA, Y.: "Arabidopsis thaliana genomic DNA, chromosome 5, P1 clone: MUF9" XP002160878 cited in the application	1,3
Y	the whole document ---	2,4
X	EMBL Database, Heidelberg, FRG Empln accession number AC007584 19 May 1999 LIN, X. ET AL.: "Arabidopsis thaliana chromosome II section 101 of 255 of the complete sequence. Sequence from clones MJB20, T19E12" XP002167059	1,3
Y	the whole document ---	2,4
X	EMBL Database, Heidelberg, FRG Emest_Pln2 accession number AI965398 24 August 1999 SHOEMAKER, R. ET AL.: "sc71b10.y1 Gm-c1016 Glycine max cDNA clone GENOME SYSTEMS CLONE ID: Gm-c1016-1844 5' similar to SW: Y506_SYNY3 Q55482 HYPOTHETICAL 28.8 KD PROTEIN SLL0506, mRNA sequence" XP002167060	1,3
Y	the whole document ---	2,4
X	EMBL Database, Heidelberg, FRG Emest_Pln2 accession number AU069089 07 June 1999 SASAKI, T.: "Oryza sativa cDNA, partial sequence (C52041_1A)" XP002160877	1
A	the whole document ---	13-15
X	EMBL Database, Heidelberg, FRG Emest_Pln4 accession number AW038635 17 September 1999 D'ASCENZO, M. ET AL.: "EST280318 tomato mixed elicitor, BTI Lycopersicon esculentum cDNA clone cLET7I9, mRNA sequence" XP002167061	1
A	the whole document --- -/--	13-15

PGP#S 00/25856

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	APFEL, C.M. ET AL.: "Use of Genomics To Identify Bacterial Undecaprenyl Pyrophosphate Synthetase" JOURNAL OF BACTERIOLOGY, vol. 181, no. 2, January 1999 (1999-01), pages 483-492, XP002160874 cited in the application	2,4
A	abstract page 486 -page 487; figure 3 page 488, column 1, line 7 -column 2, line 3 page 490, column 2, line 36 - line 64 ----	1,3,5-15
A	SHIMIZU, N. ET AL.: "Molecular Cloning, Expression, and Purification of Undecaprenyl Diphosphate Synthase" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 31, 31 July 1998 (1998-07-31), pages 19476-19481, XP002160875 cited in the application the whole document ----	1-15
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; PHYTOCHEMICAL ANALYSIS, vol. 8, no. 3, 1997 CORNISH, K. & BARTLETT, D.L.: "Stabilisation of particle integrity and particle bound cis-prenyl transferase activity in stored, purified rubber particles" XP002161336 abstract -----	1-15

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-15 partially

An isolated nucleic acid fragment encoding a plant cis-prenyltransferase polypeptide selected from the group consisting of a) an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence SEQ ID NO: 2, b) an isolated nucleic acid fragment that is substantially similar to an isolated nucleic acid fragment encoding all or a substantial portion of SEQ ID NO: 2, c) an isolated nucleic acid fragment derived from *Dimorphotheca* encoding a polypeptide having at least 41% identity with the amino acid sequence SEQ ID NO: 24, d) an isolated nucleic acid fragment derived from *Dimorphotheca* having at least 50% identity with the nucleic acid sequence SEQ ID NO: 23, e) an isolated nucleic acid fragment that hybridizes with said nucleic acid sequences, f) an isolated nucleic acid fragment that hybridizes with the nucleic acid sequence SEQ ID NO: 1, g) an isolated nucleic acid fragment that is complementary to said nucleic acid sequences, said isolated nucleic acid fragment having the nucleic acid sequence SEQ ID NO: 1, a polypeptide encoded by said isolated nucleic acid fragment, said polypeptide having the amino acid sequence SEQ ID NO: 2, a method of obtaining a nucleic acid fragment encoding all or a substantial portion of the amino acid sequence of a plant cis-prenyltransferase polypeptide comprising a hybridization step involving said nucleic acid fragment, a method of obtaining a nucleic acid fragment encoding all or a substantial portion of the amino acid sequence of a plant cis-prenyltransferase polypeptide comprising a cDNA amplification step involving primers corresponding to a portion of SEQ ID NO: 1, a chimeric gene comprising said nucleic acid fragment, a transformed host cell comprising said chimeric gene and a method of altering the level of expression of a plant cis-prenyltransferase polypeptide in a host cell;

2. Claims: 1-15 partially

Idem as subject 1 but limited to *Calendula officinalis* and SEQ ID NOS: 3 and 4;

3. Claims: 1-15 partially

Idem as subject 1 but limited to *Hevea brasiliensis* and SEQ ID NOS: 5-10;

4. Claims: 1-15 partially

Idem as subject 1 but limited to *Vitis* sp. and SEQ ID NOS:

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

11 and 12;

5. Claims: 1-15 partially

Idem as subject 1 but limited to *Oryza sativa* and SEQ ID NOS: 13-16;

6. Claims: 1-15 partially

Idem as subject 1 but limited to *Glycine max* and SEQ ID NOS: 17 and 18;

7. Claims: 1-15 partially

Idem as subject 1 but limited to *Triticum aestivum* and SEQ ID NOS: 19 and 20.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/25856

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.